



CHANDRASEKHARA et al.

Application No.: 09/380,337

Page 2

PATENT

RECEIVED

APR 26 2001

TECH CENTER 1600/2900

In the Specification:

Please insert a paragraph before the paragraph on page 1, line 1, with the following:

--CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority to U.S. Provisional Patent Application Serial No. 60/040,269, filed March 5, 1997.--

Please replace the paragraph beginning at page 3, line 4, with the following:

--Figure 2 shows the detection of frameshift and nonsense mutations. (A) Analysis of exon 2 in a MEN1 patient and a normal control, using dideoxy fingerprinting (ddF) to reveal pattern differences (arrows) indicative of a possible mutation. (B) Abnormal ddF pattern in exon 9 from a different patient. (C) Identification of a single nucleotide deletion by sequencing of a cloned exon 2 PCR product from the patient whose ddF pattern is shown in (A). The sequence shown (SEQ ID NO:4) is of the antisense strand; the mutation is 512delC (normal = SEQ ID NO:5). This frameshift mutation was confirmed by detecting the presence of a new *Afl*III site in PCR-amplified exon 2 from this patient and two affected relatives (D). (E) Direct sequencing of the exon 9 PCR product from panel (B), revealing the presence of a heterozygous C to T (C => T) substitution (SEQ ID NOS:6 and 7). Again the sequence is of the antisense strand; the mutation creates a stop codon: TGG to TAG or W436X (TGG => TAG or W436X).--

Please replace the paragraph beginning at page 18, line 3, with the following:

--In summary, the menin gene can identified and prepared by probing or amplifying select regions of a biological sample, such as a mixed cDNA or genomic pool, using the probes and primers generated from the *MEN1* sequences; exemplary probes are provided herein in Table 1 (sequence numbering based on SEQ ID NO:3):

Table 1

Exons	Primary PCR primers	Product size(bp)	ddF primers
Exon 2 from ATG	MEN2A(1932-1953) (SEQ ID NO:8) gacctgggtgcgctttctggac MEN2B(2946-2968) (SEQ ID NO:9) gaggtgaggtgatgattggag	1039	MEN2C(2451-2473) (SEQ ID NO:10) ggtagagctcgggaacgttgtag MEN2D(2629-2652) (SEQ ID NO:11) gagaccttctcaccagctcacgg MEN2E(2810-2833) (SEQ ID NO:12) cgaacctcacaaggcttacagtc MEN3C(4613-4637) (SEQ ID NO:15) ggctcttctgtcttcccttctatg
Exon 3	MEN3A(4096-4119) (SEQ ID NO:13) gttgacatagagggtgtaaacag MEN3B(5497-5520) (SEQ ID NO:14) acagttgacacaaagtgagactgg	1427	
Exon 4	MEN3A(4096-4119) (SEQ ID NO:13) gttgacatagagggtgtaaacag MEN3B(5497-5520) (SEQ ID NO:14) acagttgacacaaagtgagactgg	1427	MEN4C(4881-4904) (SEQ ID NO:16) ggtcccacagcaagtcaagtctgg
Exon 5	MEN3A(4096-4119) (SEQ ID NO:13) gttgacatagagggtgtaaacag MEN3B(5497-5520) (SEQ ID NO:14) acagttgacacaaagtgagactgg	1427	MEN5C(5138-5161) (SEQ ID NO:17) cctgttccgtggctcataactctc
Exon 6	MEN3A(4096-4119) (SEQ ID NO:13) gttgacatagagggtgtaaacag MEN3B(5497-5520) (SEQ ID NO:14) acagttgacacaaagtgagactgg	1427	MEN5C(5138-5161) (SEQ ID NO:17) cctgttccgtggctcataactctc
Exon 7	MEN7A(5828-5849) (SEQ ID NO:18) cctcagccagcagtcctgtaga MEN7B(6212-6233) (SEQ ID NO:19) ggacgaggggtggtgaaactg	408	MEN7C(5911-5933) (SEQ ID NO:20) ggactccttgggatcttctctg
Exon 8	MEN8A(6404-6425) (SEQ ID NO:21) aacgaccatcatccagcagtg MEN8B(6834-6855) (SEQ ID NO:22) ccatccctaatacccgtacatgc	454	MEN8C(6577-6600) (SEQ ID NO:23) tggtgagaccccttcagaccctac
Exon 9	MEN9A(7142-7164) (SEQ ID NO:24) ctgctaaggggtgagtaagagac MEN9B(8190-8212) (SEQ ID NO:25) ggtttgatacagactgtactcgg	1073	MEN9C(7404-7426) (SEQ ID NO:26) gtctgacaagcccgtggctgctg
Exon 10 to stop	MEN9A(7142-7164) (SEQ ID NO:24) ctgctaaggggtgagtaagagac MEN9B(8190-8212) (SEQ ID NO:25) ggtttgatacagactgtactcgg	1073	MEN10C(7445-7467) (SEQ ID NO:27) gcatctgccccatccccttcgggtg MEN10D(7775-7797) (SEQ ID NO:28) gaagcctcctgggactgtcgtg

--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 25, at the end of the application.

REMARKS

The amendment to the paragraph beginning at page 18, line 3, which includes an amended "Table 1", corrects errors in the reproduction of the table due to word processing software incompatibilities between filing of the priority application for the instant application,